UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,550	09/01/2006	Hee-Sook Song	13987-00021-US	3089

23416 7590 03/13/2008
CONNOLLY BOVE LODGE & HUTZ, LLP
P O BOX 2207
WILMINGTON, DE 19899

EXAMINER	
WORLEY, CATHY KINGDON	
ART UNIT	PAPER NUMBER
1638	
MAIL DATE	DELIVERY MODE
03/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,550	SONG ET AL.	
	Examiner	Art Unit	
	Cathy K. Worley	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *4-6,16-18,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7-15 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/1/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence alignment*.

DETAILED ACTION

Restriction/Election

1. In response to the communication received on Nov. 12, 2007 from Hui-Ju Wu, the election with traverse of group I, claims 1-3 and 7-15 (as they related to the *Pisum sativum* ptxA promoter (SEQ ID NO:1)) is acknowledged. The Applicant is reminded to amend the claims to read only on the elected promoter (the *Pisum sativum* ptxA promoter) and the elected sequence of SEQ ID NO:1.

The Applicant traverses on the grounds that Groups I, VI, VIII, and XIII all share the technical feature of using a ptxA promoter, or functional equivalent thereof (see third paragraph on page 7 of the response). This is not persuasive because part (d) of claims 1 and 16, and claims 4 and 5 are not limited in scope to the ptxA promoter or a functional equivalent thereof. These claims include the limitation of the SbHRGP3 promoter (SEQ ID NO:2) as an option for satisfying the claim. Therefore, the technical feature linking the claims is not new as evidenced by the reference by Ahn et al provided along with the restriction requirement; therefore it is not a "special" technical feature as defined by PCT Rule 13.2. The Applicant further argues that the product and process of use are an acceptable combination of categories for unity pursuant to 37 CFR 1.475 (b)(3) (see last paragraph on page 7 of the response). This is not persuasive, however, because

under unity of invention rules, the process of use is only required to be examined along with the product if the product is new and therefore is a "special" technical feature as defined by PCT Rule 13.2, in the instant case, the product is not new, and therefore, it is proper to restrict between the product and the process. This restriction requirement is **MADE FINAL.**

If the Applicant amends the claims during the course of prosecution in such a way as to distinguish the product over the prior art, then it is possible to rejoin the product and process claims. The Applicant is reminded that the examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claims 22-25 have been newly added and are drawn to the elected invention. Claims 1, 3-18, and 20-25 are pending in the instant application. Claims 4-6, 16-18, 20, and 21 are withdrawn from consideration for being directed to non-elected inventions. Claims 1, 3, 7-15, and 22-25 are examined in this Office Action.

Specification

2. The specification is objected to because this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. The Brief Description of the Drawings does not include the sequence identifiers associated with the DNA sequences depicted in figures 6, 7, and 8; and because the sequences in the Table on pages 60 and 61 do not have identifiers. Applicant is advised to

include the SEQ ID NOs: with the Brief Description of the Drawings and to amend the Table on pages 60 and 61 to include sequence identifiers. If these sequences do not already have sequence numbers assigned to them, then a sequence number must be assigned, and a new sequence listing must be submitted. The new sequences in the sequence listing must be identical to the sequences disclosed in the figures and the Table, and applicant is cautioned to avoid any new matter.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth herein. Failure to fully comply with both of these requirements in the time period set forth in this Office action will be held to be non-responsive.

3. The use of the following trademarks has been noted in this application: QIAGEN and RNEASY. They should be written in all capital letters wherever they appear; or alternatively, they should be denoted with the registered trademark symbol, ®, and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Information Disclosure Statement

4. The listing of references in the specification on pages 63-67 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

5. Claims 1, 7, and 9 are objected to because of the following informalities:

- In claim 1, there is no conjunction between parts a, b, c, and d; and the deletion of the Markush language "the group consisting of" makes the wording awkward. The Applicant is advised to put "the group consisting of" back into line 3, delete part "d)" because it is directed to a non-elected invention, and insert the conjunction - -; and - - at the end of part "b)". In addition "100 consecutive base pair" at the end of line 12 should be replaced with the plural - - 100 consecutive base pairs - - .
- In claim 7, the article "an" at the end of line 2 should be replaced with - - a - -. In addition "then" in line 4 should be replaced with - - than - - .
- In claim 9, the common at the end of line two should be deleted.

Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 3, 7-9, 11-15, and 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in this rejection; however, the limitations in claims 7 and 10 provide further clarification and therefore claims 7 and 10 are not indefinite and are not included in this rejection.

The terms "predominant" and “substantially” and “essentially” in claim 1 are relative terms which render the claim indefinite. The terms "predominant" and “substantially” and “essentially” are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The recitation in subpart i) of part c) in claim 1 does not make sense, because a 100 base pair nucleic acid can not possibly have 95% identity to SEQ ID NO:1, because SEQ ID NO:1 is 863 base pairs in length. It is unclear if the Applicant

intends to encompass any nucleic acid with 95% identity to SEQ ID NO:1, or if the Applicant intends to encompass any nucleic acid comprising a 100 base pair polynucleotide with at least 95% identity to a 100 base pair fragment of SEQ ID NO:1. For the purpose of examination, the Examiner will interpret this to mean at least 95% identity to SEQ ID NO:1. This interpretation does not relieve the Applicant of addressing this rejection under 35 USC 112, 2nd paragraph.

7. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a sequence encoding an enzyme having glucuronidase activity. The claim from which this depends does not specific what the nucleic acid of interest is, and claim 7 recites measuring glucuronidase activity. There is a missing element between the two claims.

8. Claims 1, 7-15, and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 95% identity to SEQ ID NO:1 or having a sequence that hybridizes with a fragment of at least 50 consecutive base pairs of SEQ ID NO:1 and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The Applicants describe the promoter of the Pisum sativum ptxA gene as SEQ ID NO:1 or its complement (see page 4, lines 42-43). They describe the expression patterns in transgenic Arabidopsis and canola in a Table that indicates high expression in seedlings, medium expression in leaves, roots, flowers and seed pods, and no expression in seeds for Arabidopsis; and high expression in seedlings and leaves, medium expression in flowers, low expression in seed pods, and no expression in seeds for Canola (see Table 1 on page 56). The construct in Example 2 is presumed to comprise SEQ ID NO:1, although this is not expressly stated in the specification. They describe motifs that were identified using computer analysis of the nucleotide sequence of SEQ ID NO:1 (see pages 59-60). They describe a construct comprising a chimeric promoter comprising the ptxa promoter and the maize ubiquitin intron, and they describe the expression pattern from this chimeric promoter as high in embryogenic calli and *in vitro* root, and medium in *in vitro* leaves and plantlets (see Example 17 and Table 3 on page 62).

The essential feature of the promoter recited in the instant claims is that it has promoter activity that is functionally equivalent to SEQ ID NO:1.

They do not describe expression patterns for transformed maize past the T_o plantlet stage. They do not describe any functional equivalent homologs of SEQ ID NO:1. They do not describe any nucleic acids with 95% identity to SEQ ID NO:1 or that hybridize to SEQ ID NO:1 that retain promoter activity, other than the nucleic acid of SEQ ID NO:1 itself.

The recitation of a sequence having at least 95% identity to SEQ ID NO:1 and the recitation of a sequence that hybridizes to a 50 bp fragment of SEQ ID NO:1 encompass nucleic acids having additions, deletions, substitutions or insertions relative to SEQ ID NO:1. The Applicants do not describe any additions, deletions, substitutions, or insertions within SEQ ID NO: 1 that retain promoter activity equivalent to the promoter activity of SEQ ID NO:1. Further the specification does not describe any DNA molecules that hybridize under high stringency conditions to a 50 bp fragment of SEQ ID NO:1 that retain promoter activity equivalent to the promoter activity of SEQ ID NO:1.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See

University of California v. Eli Lilly and Co., 119 F. 3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Applicants fail to describe a representative number of nucleic acid molecules with promoter activity that comprise a nucleotide sequence with additions, deletions, substitutions or insertions into SEQ ID NO:1 or a nucleic acid that hybridizes to a 50 bp fragment of SEQ ID NO:1. The Applicants only describe the nucleic acid of SEQ ID NO:1 which was shown to have promoter activity in transgenic plants. Furthermore, the Applicants fail to describe structural features common to members of the claimed genus of nucleic acids that are sufficient for having promoter activity equivalent to the promoter activity of SEQ ID NO:1. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for promoter activity equivalent to the promoter activity of SEQ ID NO:1, it remains unclear what features identify nucleic acids capable of such activity. Since the genus of nucleic acids has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Isolated nucleic acids that have at least 95% identity with SEQ ID NO:1 encompass over 4^{43} (or, written in scientific notation, 7.7×10^{25}) nucleotide molecules with additions, deletions, substitutions or insertions into SEQ ID NO:1. The recitation of a nucleic acid that hybridizes to a 50 bp fragment of SEQ ID NO:1

encompasses numerous molecules that also have additions, deletions, substitutions or insertions into SEQ ID NO:1. These recitations encompass multitudes of molecules, many of which would not comprise promoter activity equivalent to the activity of SEQ ID NO:1, and most of which were not in the possession of the Applicant at the time of filing. The Applicants have reduced to practice only one promoter (presumed to be SEQ ID NO:1) in an experiment that demonstrates promoter activity. Accordingly, the specification fails to provide an adequate written description to support the genus of nucleic acids with promoter activity equivalent to SEQ ID NO:1 that comprise a nucleotide sequence with 95% identity to SEQ ID NO:1 or a nucleic acid that hybridizes to a 50 bp fragment of SEQ ID NO:1 as set forth in the claims. (See Written Description guidelines published in the Federal Register/Vol. 66, No. 4/Friday, January 5, 2001/Notices: p. 1099-1111).

9. Claims 1, 3, 7-15, and 22-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a promoter comprising a fragment of SEQ ID NO:1 wherein said fragment comprises promoter activity in a plant, and wherein the promoter activity is higher in vegetative tissues of Arabidopsis or canola than in seeds of Arabidopsis or canola, and for constructs, vectors, host cells, plants, cell cultures, parts, and propagation material comprising said promoter, does not reasonably provide enablement for a promoter comprising a nucleic acid having 95% identity to SEQ ID NO:1, or comprising a polynucleotide

that hybridizes to a 50 bp fragment of SEQ ID NO:1, or comprising the complement of SEQ ID NO:1, or for promoter activity in substantially all vegetative tissues of any plants other than Arabidopsis and canola, and for constructs, vectors, host cells, plants, cell cultures, parts, and propagation material comprising said promoter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The nature of the invention is a molecular biological approach for the heterologous expression of recombinant proteins in transgenic plants.

The claims are broadly drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 95% identity to SEQ ID NO:1 or having a sequence that hybridizes with a fragment of at least 50

consecutive base pairs of SEQ ID NO:1 and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The Applicants teach the promoter of the Pisum sativum ptxA gene as SEQ ID NO:1 or its complement (see page 4, lines 42-43). They teach that the expression patterns in transgenic Arabidopsis and canola transformed with a construct comprising the ptxA promoter is high expression in seedlings, medium expression in leaves, roots, flowers and seed pods, and no expression in seeds for Arabidopsis; and high expression in seedlings and leaves, medium expression in flowers, low expression in seed pods, and no expression in seeds for Canola (see Table 1 on page 56). The construct in Example 2 is presumed to comprise SEQ ID NO:1, although this is not expressly stated in the specification. They teach motifs that were identified using computer analysis of the nucleotide sequence of SEQ ID NO:1 (see pages 59-60). They teach a construct comprising a chimeric promoter comprising the ptxA promoter and the maize ubiquitin intron, and they teach that the expression pattern from this chimeric promoter is high in embryogenic calli and *in vitro* root, and medium in *in vitro* leaves and plantlets (see Example 17 and Table 3 on page 62).

They do not teach expression patterns for transformed maize past the T_o plantlet stage. They do not teach any functional equivalent homologs of SEQ ID NO:1. They do not teach any nucleic acids with 95% identity to SEQ ID NO:1 or that hybridize to SEQ ID NO:1 that retain promoter activity, other than the nucleic

acid of SEQ ID NO:1 itself. They do not teach any expression pattern for a construct comprising only the fragment of SEQ ID NO:1 from position 300 to 583 of SEQ ID NO:1 (as claimed in claim 3). They do not teach expression patterns in any plants other than Arabidopsis, Canola, and T_o maize plantlets.

The recitation of a sequence having at least 95% identity to SEQ ID NO:1 and the recitation of a sequence that hybridizes to a 50 bp fragment of SEQ ID NO:1 encompass nucleic acids having additions, deletions, substitutions or insertions relative to SEQ ID NO:1. The Applicants do not teach any additions, deletions, substitutions, or insertions within SEQ ID NO:1 that retain promoter activity equivalent to SEQ ID NO:1. Further the specification does not teach any nucleic acids that comprise the sequence of the complement of SEQ ID NO:1 that retain promoter activity.

The state-of-the-art is such that one of skill in the art cannot predict which additions, deletions, substitutions, or insertions within a full-length promoter can be tolerated such that the promoter retains its activity. Mutation of promoter sequences produces unpredictable results. Donald et al (1990, EMBO J. 9:1717-1726) in a mutational analysis of the *Arabidopsis rbcS-1A* promoter found that the effect of a particular mutation was dependent on promoter fragment length (paragraph spanning pg 1723-1724). The region of a given promoter that has a specific activity cannot be predicted and involves the complex interaction of different subdomains (Benfey et al, 1990, Science 250:959-966, see Abstract, Fig. 3-

5). Even a very small region may be critical for activity, and the criticality of a particular region must be determined empirically (Kim et al, 1994, Plant Mol. Biol. 24:105-117, Tables 1-4, Abstract, Fig. 1-2).

In addition, the promoter of this invention, the ptxA promoter from *Pisum sativum* (SEQ ID NO:1), was discovered and sequenced by David Phillip Bown, and published in his Ph.D. dissertation in 1992 (see Bown, D. P. Thesis, Dept. of Biol. Sci., Univ. of Durham, Durham, UK (1992)). Bown also deposited the complete genomic sequence, including the promoter, in GenBank Accession X67427 (1997). Bown conducted experiments to determine the expression patterns of the endogenous ptxA gene in *Pisum Sativum*, and he determined that it was expressed strongly in pods, but not in leaves, and only weakly in petals (see second paragraph on page 126; pPP590 is the clone of the ptxA gene). Given this prior art teaching which is in complete opposition to the expression patterns disclosed in Arabidopsis and canola in the instant specification, it is clear that the tissue-specificity of expression from this promoter is different in different plant species. Bown teaches that there is a very close homolog in tomato which is expressed at high levels in young tomato fruit and low in stem, root, etiolated seedlings, leaf, and mature-green and ripe fruits (see paragraph bridging pages 158-159); therefore, one would predict that the ptxA promoter might drive expression predominantly in young tomato fruit if transformed into a tomato plant. Given this high degree of unpredictability, claims to a particular tissue-specificity are only enabled for the plants in which a

tissue specificity has been determined. Note that the experiments in transgenic maize did not proceed past T_o plantlets, therefore, tissue-specificity in stably-transformed maize plants was not determined in the instant application. Note that the fragment recited in claim 3 has not been disclosed to have a particular tissue-specificity in any plant.

In addition, claim 13 recites yeast, algae, and fungi host organisms; and one of skill in the art would not know how to use a yeast, algae or fungi transformed with a construct comprising the ptxA promoter. The ptxA promoter is unlikely to be active in yeast, algae, or fungi given that it is a plant promoter with tissue-specificity that appears to be dependent on the species of plant in which it is integrated. Therefore, one of skill in the art would not know how to use a yeast, algae, or fungi transformed with a construct comprising an inactive promoter.

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of skill in the art to make multitudes of additions, deletions, substitutions, and insertions and test each one for promoter activity and determine what tissues the promoter drives expression in for each species of plant. Furthermore, a nucleic acid with substitutions would have the property of hybridizing to 50 bp fragments of SEQ ID NO:1 under stringent conditions, and there is a high degree of unpredictability about which substitutions or deletions would be tolerated.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to make and use the claimed invention, and therefore, the invention is not enabled throughout the broad scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 3, 7-15, and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Donald et al (The EMBO Journal (1990) Vol. 9, pp. 1717-1726).

The claims are drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having a sequence that hybridizes with a fragment of at least 50 consecutive base pairs of SEQ ID NO:1 and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

Donald et al teach constructs comprising the rbcS-1A promoter operably linked to a nucleic acid of interest encoding ADH (see entire article). They also produce constructs with the GUS reporter gene (see paragraph bridging pages 1722-1723). The rbcS-1A promoter has the inherent property of hybridizing under some

stringency conditions with a fragment of SEQ ID NO:1, and because the hybridization conditions have not been defined, they have only been exemplified in the specification, then any hybridization conditions are encompassed by the instant claims. The constructs taught by Donald et al comprise a sequence from "about" base pair 300 to "about" base pair 583 of the sequence described by SED ID NO:1 (see bases 575-580 of the instant SEQ ID NO:1 and see bases -310 to -305 in Figure 3 on page 1720). The Examiner interprets 575 to be "about" 300 and 580 to be "about" 583.

Donald et al teach that their constructs produce leaf-specific expression in transgenic tobacco plants (see second paragraph in the left column and right column on page 1718 and Figure 4 on page 1720 and Figure 5 on page 1721), and tobacco plants are non-human organisms and are dicots. Although Donald et al did not specifically measure the β-glucuronidase (GUS) activity in seeds and flower tissue; the construct they taught would have the inherent property of having less than 10% of the expression in seeds and flowers compared to vegetative plant tissues, because the promoter they taught is regulated in a light regulated and leaf-specific manner.

Some of the constructs taught by Donald et al comprise portions of the Adh promoter and leader in addition to the rbcS-1A promoter (see left column on page 1718); therefore they comprise additional functional elements. The construct taught by Donald et al comprises the coding region of ADH in sense orientation which results in expression of the ADH protein (see Figure 1 on page 1718 and

Figure 2 on page 1719). The constructs taught by Donald et al have expression in leaves (see Figure 4 on page 1720). Some of the constructs showed enhanced root expression (see Figure 5 and last paragraph on page 1721). Although they did not measure the expression in stems and seeds, the construct taught by Donald et al has the inherent property of expressing in stems, because the promoter is light regulated, and it has the inherent property of not expressing in seeds, because seeds are not exposed to light. Donald et al teach that their constructs are inserted into a binary vector (pEnd4k) (see last paragraph on page 1724). They teach seeds of the transgenic tobacco plants (seed third paragraph in the right column on page 1725), and these seeds are "parts" and are "propagation material" derived from the transgenic organism.

11. Claims 15 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Khan A. A. (US Patent No. 5,294,593, issued on Mar. 15, 1994).

The claims are drawn to a cell culture, part, or transgenic propagation material derived from a transgenic organism comprising an expression construct comprising a functional equivalent of the ptxA promoter.

Khan teaches a seed (see columns 4-11 and all claims) which is a "part" of a plant. Because the non-human transgenic organism recited in claims 12 and 13 can be a transgenic plant that is heterozygous for the expression cassette, seeds produced by the plant may not comprise the nucleic acid molecule. 50% of seeds

produced from crossing a heterozygous transgenic plant with a wild-type plant do not comprise the transgene, and 25% of seeds produced from self-pollination of a heterozygous transgenic plant do not comprise the transgene. Therefore, the seeds taught by Khan are indistinguishable from non-transgenic seeds encompassed by the instant claims 15 and 24. The Applicant is advised to amend the claims to include - - ; wherein said cell culture, part, or propagation material comprises said construct - - . This amendment would overcome this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 3, 8-15, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henkes et al (US 2003/0140380, published on Jul. 24, 2003; and filed as App. No. 10/293,958 on Nov. 12, 2002, with priority to Nov. 9, 2001) as evidenced by Bown, D.P. (GenBank Accession X67427, published on Oct. 29, 1997; pp. 1-3).

The claims are drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 95% identity to SEQ ID NO:1 or

having a sequence that hybridizes with a fragment of at least 50 consecutive base pairs of SEQ ID NO:1 and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The instant claims are obvious over the prior art because there was some teaching, suggestion, or motivation in the knowledge generally available to one of ordinary skill in the art to combine the reference teachings, and there was a reasonable expectation of success in combining the teachings.

SCOPE AND CONTENT OF THE PRIOR ART – PRIMARY REFERENCE

Henkes et al teach a construct comprising a "super promoter", a "desired gene", and the NOS polyadenylation signal (see Figure 1). They teach a transgenic plant comprising this construct; including monocots and dicots (see claims 9-12). They teach seeds which are "parts" of plants and are "propagation material" derived from the transgenic plants (see claims 15 and 16). They teach the use of a binary vector for transformation of plants (see paragraph 0098 on page 14). They teach the PtxA promoter from GenBank Accession # X67427 as a stress inducible promoter, and they suggest that it can be used in one of the preferred embodiments of their invention (see paragraph 0107 on page 16).

DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE TEACHINGS OF HENKES ET AL

Henkes et al do not teach the sequence of SEQ ID NO:1, nor do they teach any particular tissue specificity of expression.

SCOPE AND CONTENT OF THE PRIOR ART – SECONDARY REFERENCE

Bown teaches the ptxA promote (see GenBank Accession X67427) which comprises a sequence that is 100% identical to the instant SEQ ID NO:1 (see sequence alignment).

LEVEL OF ORDINARY SKILL IN THE PERTINANT ART

The pertinent art is the field of molecular biology, and one of ordinary skill in this art would have earned a Ph.D. in molecular biology, biochemistry, plant biology, or some other related field; as evidenced by the skill level of Bown and Henkes, and the co-authors/co-inventors of Henkes. One of ordinary skill in this art would have been well-versed in techniques for heterologous expression of recombinant proteins and would be familiar with the literature encompassing different inducible plant promoters and would appreciate the utility of stress-inducible expression of recombinant proteins.

FINDING OF OBVIOUSNESS

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Henkes et al and Bown. These teachings include each element recited in the instant claims, with the exception of the particular tissue-specificity recited. Because Henkes et al teach that it is a preferred embodiment to utilize a stress-inducible promoter and they specifically suggest the PtxA promoter taught by Bown (see paragraph 0107 on page 16), one of ordinary skill in the art would have been motivated to combine the

teachings of Bown and Henkes to arrive at the instant invention. One would have had a reasonable expectation of success for expressing recombinant proteins in response to stress in plants transformed with the construct.

The property of expressing predominantly in leaves in Arabidopsis and canola is an intrinsic property of the ptxA promoter, and therefore, although Bown and Henkes do not teach this property, it would naturally flow from the combination of Henkes et al and Bown. A mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. See *In re Baxter Travenol Labs.*, 952 F.2d 388, 21 USPQ2d 1281 (Fed. Cir. 1991), where the court held that the fact that another advantage would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

For these reasons, the instant claims are obvious over the prior art.

13. Claims 1, 3, 8-15, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arntzen et al (US Patent No. 6,395,964; issued on May 28, 2002) in view of Bown, D.P. (Thesis, Dept. of Biol. Sci., Univ. of Durham, Durham, UK (1992)), as evidenced by Bown, D.P. (GenBank Accession X67427, published on Oct. 29, 1997; pp. 1-3).

The claims are drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 95% identity to SEQ ID NO:1 or

having a sequence that hybridizes with a fragment of at least 50 consecutive base pairs of SEQ ID NO:1 and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The instant claims are obvious over the prior art because there was some teaching, suggestion, or motivation in the knowledge generally available to one of ordinary skill in the art to combine the reference teachings, and there was a reasonable expectation of success in combining the teachings.

SCOPE AND CONTENT OF THE PRIOR ART – PRIMARY REFERENCE

Arntzen et al teach transgenic plants expressing oral antigens for use in oral immunization of animals (see entire document). They teach that the plant that expresses the antigen acts as both as an immunogen and an adjuvant, and that the transgenic plant material can be fed to animals (see abstract). They teach that the plants can be monocots; such as corn, rice, barley, wheat and rye; and dicots; such as sunflower, soybean, cotton, rapeseed, and tobacco (see second paragraph in column 7), and that the protein expressed by the transgenic construct should be expressed in edible transgenic plant tissues (see lines 45-50 in column 9); these edible tissues are "parts" derived from the transgenic plants. Arntzen et al teach vectors that comprise expression cassettes comprising promoters operably linked to coding sequences and further comprising polyadenylation signals which are additional functional elements (see Figure 1).

DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE TEACHINGS OF ARNTZEN ET AL

Arntzen et al do not teach the ptxA promoter, nor do they teach expression in vegetative tissues without expression in seeds, nor do they teach expression of GUS.

SCOPE AND CONTENT OF THE PRIOR ART – SECONDARY REFERENCE

Bown teaches the ptxA promoter (see pages 129-131 – note that ptxA is designated as pPP590) which is 100% identical to the instant SEQ ID NO:1 as evidenced by GenBank Accession X67427 (see sequence alignment). Bown conducted experiments to determine the expression patterns of the endogenous ptxA gene in *Pisum Sativum*, and he determined that it was expressed strongly in pods, but not in leaves, and only weakly in petals (see second paragraph on page 126; pPP590 is the clone of the ptxA gene). Bown teaches that there is a very close homolog in tomato which is expressed at high levels in young tomato fruit and low in stem, root, etiolated seedlings, leaf, and mature-green and ripe fruits (see paragraph bridging pages 158-159); therefore, one would predict that the ptxA promoter would drive expression predominantly in young tomato fruit if transformed into a tomato plant.

LEVEL OF ORDINARY SKILL IN THE PERTINANT ART

The pertinent art is the field of molecular biology, and one of ordinary skill in this art would have earned a Ph.D. in molecular biology, biochemistry, plant biology, or some other related field; as evidenced by the skill level of Bown and

Arntzen, and the co-authors/co-inventors of Arntzen. One of ordinary skill in this art would have been well-versed in techniques for heterologous expression of recombinant proteins and would be familiar with the literature encompassing different tissue-specific plant promoters and would appreciate the utility of tissue-specific expression of recombinant proteins.

FINDING OF OBVIOUSNESS

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Arntzen et al and Bown. These teachings include each element recited in the instant claims, with the exception of the particular tissue-specificity recited. Because Arntzen et al teach that it would be beneficial to express recombinant immunogens in edible plant parts, one of ordinary skill in the art would have been motivated to combine the teachings of Bown and Arntzen to arrive at the instant invention.

Bown teaches the ptxA promoter and teaches that the expression of ptxA in peas is predominantly in the seed pods which is the edible portion of the plant; and Bown teaches that the closest homolog is in tomato where it is expressed predominantly in young fruit which is an edible portion of the tomato plant, therefore, one of ordinary skill in the art would have been motivated to utilize the promoter taught by Bown in the invention taught by Arntzen et al to arrive at the instant constructs, vectors, and host cells. One would have had a reasonable

expectation of success for expressing recombinant proteins in seed pods and young fruits of plants transformed with the construct.

The property of expressing predominantly in leaves in Arabidopsis and canola is an intrinsic property of the ptxA promoter, and therefore, although Bown does not teach this property, it would naturally flow from the combination of Arntzen et al and Bown. A mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. See *In re Baxter Travenol Labs.*, 952 F.2d 388, 21 USPQ2d 1281 (Fed. Cir. 1991), where the court held that the fact that another advantage would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

For these reasons, the instant claims are obvious over the prior art.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/
Cathy K. Worley
Patent Examiner
Art Unit 1638

CKW